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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/891,206	06/26/2001	Nigel D. Atherton	PHARMA-131	9337

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EXAMINER
PAK, JOHN D

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 01/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/891,206	Atherton et al.
Examiner	**Art Unit**
John Pak	1616

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Nov 4, 2002*

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above, claim(s) *22, 25, and 33* is/are withdrawn from consideratio

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-21, 23, 24, 26-32, and 34-37* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examine

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☒ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *6,7*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Claims 1-37 are pending in this application.

Applicant's election of lanthanum carbonate as the single disclosed species in Paper No. 9 (11/4/02) is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a). Applicant is advised that the elected species that will be examined herein is expanded to include the following: all lanthanum (III) simple binary salts such as lanthanum carbonate and $LaCl_3$.

It is noted for the record that Examiner Pak telephoned Mr. Heaney on 1/17/03 for the following further modification of the restriction requirement:

Group I, claims 1-21, 23-32 and 34-37, directed to various methods comprising administering lanthanum (III) compound.

Group II, claims 22 and 33, directed to a composition for the treatment or prevention of a bone remodeling disorder comprising a lanthanum compound and a bone enhancing agent.

Inventions of Group I and Group II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the product as claimed can be used in nutritional supplementation.

In addition to distinctness of the two inventions, there would be an undue burden placed on the Examiner if the restriction were not required. Group II would necessitate searching in places where no pertinent art to the various methods of Group I would be found. As Group II composition invention is readable on various nutritional supplements and other unrelated compositions, the search for the two inventions would be clearly divergent. In view of the already extensive burden placed on the Examiner in having to search and examine the various methods of Group I, to search and examine the composition invention of Group II would amount to undue burden.

Therefore, for the reasons of distinctness and undue burden, the restriction requirement as set forth above is deemed to be proper.

During a telephone conversation on 1/22/03, Mr. Heaney elected with traverse Group I, and maintained the species election of lanthanum carbonate from Paper No. 9 (11/4/02).

Accordingly, claims 22 and 33 are withdrawn from further consideration as being directed to non-elected subject matter, and claims 1-21, 23-32 and 34-37 will presently be examined to the extent that they read on the elected subject matter as noted above.

Claims 20-21 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 20-21 provide for the use of a lanthanum III compound, but, since the claims do not set forth any steps involved in the method/process, it is

unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. Claim 25 is slightly different in language in that it is claimed as the use of a compound in the method of claim 1. However, the same indefiniteness issue is raised because the "use" that is claimed in claim 25 is still without specific steps since said use could be myriad other uses unrelated to the method of claim 1.

Claims 20-21 and 25 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966). As noted above with respect to claim 25, the language there is readable on any "use" of a lanthanum since claim 25 reads on taking the lanthanum compound of claim 1 and using it for any other unspecified purpose, without specific method steps.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 9-11, 13-17, 23-24, 26-32, 34-35 are rejected under 35 U.S.C. 102(b) as being anticipated by Hutchison (Ref. no. 13 on PTO-1449 of 5/9/02).

Hutchison explicitly discloses administering lanthanum as lanthanum carbonate in multiple doses up to 4.5 g to healthy male volunteers in a Phase I trial and doses up to 2.25 g per day to CAPD patients in a Phase II trial (p. S410, left column). Lanthanum carbonate is a phosphate binder (*id.*). Management of renal osteodystrophy is disclosed (title).

With respect to Hutchison's healthy male volunteers, enhancement of bone formation would necessarily have been obtained because applicant's claim 1 requires no more than administering a lanthanum (III) compound, i.e.Hutchison's lanthanum carbonate, to a human in need thereof (and all humans would appear to be covered by "in need thereof").

Although the specific disorders recited in the claims and the specific activity recited in the claims are not specifically disclosed by the cited reference, the same lanthanum (III) compound was administered to dialysis patients who are known to be at risk for osteodystrophy and various other bone disorders due to abnormal blood chemistries. For example, in certain cases renal osteodystrophy is referred to as "renal rickets" and renal osteodystrophy is known to be a risk for osteoporosis[1]. Therefore, because the same lanthanum carbonate was administered to humans and at-risk humans, the same end result would necessarily be obtained due to the fact that the claimed method steps read on the method steps disclosed by the cited reference. See,

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[1] Renal Osteodystrophy, retrieved from the Internet. [URL: www.niddk.nih.gov].

e.g., In re May, 197 USPQ 601, 607 (CCPA 1978); Ex parte Novitski, 26 USPQ2d 1389, 1390-91 (Bd. Pat. App. & Int. 1993); In re Kirby, 40 USPQ 368 (CCPA 1939).

Claim 15 is rejected under 35 U.S.C. 102(b) as being anticipated by Shankar et al. (Ref. no. 15 on PTO-1449 of 6/9/02).

Shankar et al. explicitly disclose contacting osteoclasts with a lanthanum (III) compound, $LaCl_3$. See pages 907-908, in particular the Materials and Methods section, page 908, first full paragraph. La^{+3} elevates cytosolic $[Ca^{+2}]$, which inhibits osteoclastic bone resorption (p. 907, first full paragraph; see also first three paragraphs of the Discussion section on p. 911). The same osteoclast is contacted with the same lanthanum (III) compound in Shankar's disclosure, and therefore the same effect as that claimed in claim 15 would necessarily be obtained. Claim 15 is thereby anticipated.

Claims 1, 13-17, 23-24 are rejected under 35 U.S.C. 102(b) as being anticipated by Harris et al. (Ref. no. 18 on PTO-1449 of 5/9/02).

Harris et al. explicitly disclose administering $LaCl_3$ to rachitic rats (p. 276, last paragraph). $LaCl_3$ is disclosed to enhance in vitro calcification (see the entire article). Although the specific results recited in applicant's claims are not specifically disclosed by the cited reference, the same lanthanum (III) compound was administered to a mammal with rickets. The same end result would necessarily be obtained because the claimed method steps read on the

method steps disclosed by the cited reference. See, e.g., May, 197 USPQ at 607; Novitski, 26 USPQ2d at 1390-91; Kirby, 40 USPQ at 368.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-19, 23-24, 26-32, 34-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hutchison in view of Fernandez-Gavarron et al. (Ref. no. 8 on PTO-1449 of 5/9/02).

Hutchison explicitly discloses administering lanthanum as lanthanum carbonate in multiple doses up to 4.5 g to healthy male volunteers in a Phase I trial and doses up to 2.25 g per day to CAPD patients in a Phase II trial (p. S410, left column). Lanthanum carbonate is a phosphate binder (*id.*). Management of renal osteodystrophy is disclosed (title).

Fernandez-Gavarron et al. teach that lanthanum ions are taken up by teeth, bone and hydroxyapatite, and the exchange of lanthanum for calcium increases resistance of the hard tissues to acid dissolution (see Summary on p. 283; pp. 286-290, in particular Table 1 on p. 286; Conclusion nos. 2 and 3 on pp. 290-291).

With respect to claims 1-5, 9-11, 13-17, 23-24, 26-32, 34-35, these claims have already been rejected under 35 USC 102(b) over Hutchison; and therefore, there is no patentable difference between said claims and Hutchison.

Claims 6 and 7 require that the human subject "has a bone remodelling disorder is at risk of developing such disorder," wherein the disorder is osteoporosis, or more specifically, primary osteoporosis, secondary osteoporosis, post-menopausal osteoporosis, male osteoporosis and steroid induced osteoporosis. It would have been obvious to the ordinary skilled artisan in this field, who is a highly trained medical professional with the responsibility for patient management and therapy, that Hutchison's dialysis patients, who are at risk for renal osteodystrophy, are also at risk for other bone disorders such as osteoporosis and its various specific forms, particularly in the case of older dialysis patients or female dialysis patients who have undergone menopause, because the cause of renal osteodystrophy (e.g. hyperphosphatemia) also increases the risk of such other bone diseases like osteoporosis.

Claim 8 requires a human subject with a bone fracture, bone trauma, or conditions associated with post-traumatic bone surgery, post-prosthetic joint surgery, post-plastic bone surgery, post-dental surgery, bone chemotherapy treatment or bone radiotherapy treatment. Although Hutchison's dialysis patients are not expressly disclosed as having such conditions or ailments, given the state of their health and bones from being on dialysis, at least "bone trauma" or bone fracture would have been fairly encompassed by such a patient group. It would have been obvious to the ordinary skilled artisan that dialysis patients who additionally suffer bone

problems of the type recited in instant claim 19 should continue with Hutchison's lanthanum carbonate therapy because of its management of the bone-weakening osteodystrophy and the expectation from Fernandez-Gavarron et al. that lanthanum ions would further strengthen bones.

Claim 12 recites 0.1 to 10 mg of lanthanum (III) compound/kg/day. For a 75 kg patient, this comes out to 0.75 mg/day, maximum. Hutchison discloses "up to 2.25 g per day" in a Phase II trial. One having ordinary skill in the art would recognize that lower doses were administered in the Phase II trial, and would have been motivated to lower the dose as claimed to suit the specific severity of the need to manage renal osteodystrophy and patient tolerability on a case by case basis.

Claims 18 and 19 are directed to enhancing bone formation by administering a lanthanum (III) compound in combination with at least one bone other bone enhancing agent, e.g. vitamin D analog. Hutchison discloses the well known fact that patients undergoing dialysis require additional vitamin D_3 (see the paragraph bridging the two columns on page S410). Therefore, one having ordinary skill in the art would have been motivated to administer both lanthanum carbonate and vitamin D_3 to dialysis patients at risk for bone disorders, such as those disclosed by Hutchison.

Claims 36 and 37 recite lanthanum carbonate in the form of hydrates. One of ordinary skill in the art would recognize lanthanum carbonate hydrates as equivalents to lanthanum carbonate. Therefore, the ordinary skilled artisan would have been motivated to utilize any one

of lanthanum carbonate, lanthanum hydrate, or lanthanum tetrahydrate with the expectation that the same therapeutic result would be obtained.

Therefore, the claimed invention, as a whole, would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention and the claimed invention as a whole have been fairly suggested by the teachings of the cited references.

A facsimile center has been established in Technology Center 1600. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier numbers for accessing the facsimile machines are (703) 308-4556 or (703) 305-3592.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Examiner Pak whose telephone number is (703) 308-4538. The Examiner can normally be reached on Monday through Friday from 7:30 AM to 4 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Mr. José Dees, can be reached on (703) 308-4628.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

JOHN PAK
PRIMARY EXAMINER
GROUP 1600